REVIEW ARTICLE

Clinical Applications of Neurostimulation: Forty Years Later

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■ **Abstract:** With the recent technological advances, neurostimulation has provided new hope for millions of patients with debilitating chronic pain conditions that respond poorly to other therapies. Outcome research demonstrated that patients with failed back surgery syndrome and complex regional pain syndromes benefit significantly from neurostimulation in pain reduction, functional capacity, and quality of life. Increasing clinical evidence supports the use of neurostimulation in post-herpetic neuralgia, peripheral neuropathy, occipital neuralgia, and other neuropathic pain conditions. Strong clinical evidences indicate that neurostimulation offers less invasive and more effective therapies for many patients with ischemic pain caused by cardiovascular and peripheral vascular diseases. A growing body of literature supports neurostimulation for visceral pain in general and interstitial cystitis in particular. As a basic principle, patient selection for the appropriate neurostimulation modalities is essential for safe, efficacious, and cost-effective applications of this therapy. Research with more vigorous designs is needed to establish evidence-based applications of neuromodulation therapy in emerging indications of pain management. ■

Key Words: spinal cord stimulation, back pain, central nervous system stimulation, complex regional pain syndrome, review, failed back surgery syndrome, visceral pain, ischemic pain

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INTRODUCTION

The field of neurostimulation has grown dramatically in recent decades, 40 years after Shealy et al. implanted the first neurostimulator in 1967.[1] As many as 50,000 neurostimulators are implanted worldwide each year for a variety of indications. Over the past few years, tremendous advances have been made in the technology along with the emergence of new indications for neurostimulation. This article reviews the evidence with respect to clinical applications of neuromodulation in pain management.

FAILED BACK SURGERY SYNDROME

In the U.S. alone, more than 1,100,000 patients undergo spine surgery each year. Unfortunately, as many as 40% of these patients will not get the desired outcome and experience chronic pain afterwards.[2] Some of these patients will carry the diagnosis of failed back surgery syndrome (FBSS), characterized by intractable chronic

pain that may affect the legs, buttocks, or low back. The name of this condition may lack precision since the surgery might have succeeded in correcting the underlying spine pathology while failing to achieve adequate long-term pain relief. In the U.S., FBSS is the most common indication for neurostimulation therapy.[3] Patients with chronic pain after multiple back operations often suffer from depression, impaired functional abilities, loss of employment, poor sleep, and several other comorbidities. Among the sources of the FBSS pain are recurrence of disc herniation, arachnoiditis, epidural fibrosis, and various radiculopathies.[4]

FBSS is typically managed with conservative medical treatments such as medications, physical therapy, selective nerve root blocks, and epidural steroid injections. Patients who do not respond to these treatments may be recommended for neuromodulation therapy, or more specifically, spinal cord stimulation (SCS). SCS involves placing one or more multiple contacts neurostimulation leads into the posterior epidural space of the spine to create an electric field over the cord dorsum of the spinal cord. Careful targeting of the appropriate spinal levels results in paresthesia in the painful areas of the body. The success of SCS for FBSS patients is influenced by several factors including: the exact pathology and type of pain generator, how much of the pain is neuropathic, and the patient's motivations and active participation. Timely application of the therapy is another very important factor. The best results are seen when the therapy is administered to patients within 3 years of their initial back surgery.[5]

Many studies, mostly in the form of retrospective case series and a few prospective, have been published consistently showing the benefits of neurostimulation therapy to treat FBSS.[6–10] The majority of FBSS patients report at least a 50% reduction in pain when treated with SCS, as well as functional improvement and a greater likelihood of returning to work.[10–12] Despite these investigations and a wealth of clinical experience regarding this application of SCS, only two randomized, controlled study has been performed to evaluate the therapy's effectiveness in treating FBSS patients. The first study compared the clinical outcomes of SCS and repeated back surgeries and found that patients treated with SCS reported better pain relief and higher satisfaction levels than those treated with surgical reoperations, and when given the choice, many patients who received reoperations would choose SCS over reoperation.[13] The second study compared the outcomes of conventional medical management (CMM) alone vs. SCS plus CMM in 100 patients with FBSS and predominantly radicular leg pain.[14] The SCS group experienced better leg and back pain relief, improved functional capacity and quality of life, as well as greater treatment satisfaction. In the intention-to-treat analysis at 6 months, 24 SCS patients (48%) and 4 CMM patients (9%) achieved the primary outcome, ≥50% pain reduction. Between 6 and 12 months, 5 SCS patients crossed over to CMM and 32 CMM patients crossed over to SCS. However, 27 SCS patients (32%) had experienced device-related complications at 12 months.

FBSS pain is frequently located in both the low back and legs, with the former being historically more challenging to treat than the latter. This is partly due to the anatomy of the spinal cord at the thoracic levels that contain the nerve targets related to the low back pain.[15] These targets consist of dorsal column tracts that are adjacent to dorsal root nerves entering the dorsal horn of the spinal cord. The proximity of these structures to one another can create a challenge when applying SCS, as stimulation of the dorsal root nerves can lead to dysesthesia or unpleasant motor responses. Besides the issue of proximity is the special orientation of the dorsal root nerves, which makes them easier to stimulate than dorsal column nerves. This problem is compounded by the relative thickness of the cerebral spinal fluid layer at the thoracic spinal cord, which increases the stimulus amplitudes required to reach the spinal cord targets, again raising the possibility of unintentional stimulation of the dorsal root nerves. For these reasons the SCS leads should be positioned close to the midline. It should be noted that the spinal cord midline may not be reliably reflected by the radiographic images, particularly in patients with scoliosis.

Recently, advances in SCS technology have allowed better coverage of the back and patients are reporting better outcomes and more relief of their back pain.[16] Studies are currently being conducted to test newer technologies to treat patients whose pain is predominantly in the back. SCS is preferred over the intrathecal drug delivery systems as it could reduce or spare the patients from the consequences of long-term opioid use.[17] Peripheral nerve and peripheral nerve field stimulation, two newer types of neurostimulation, may be combined with SCS to improve the outcomes of patients with low back pain.[18] More studies are needed to determine the efficacy of these stimulation modalities.

Repeated surgeries have a poor record of pain relief for FBSS patients, even though in some circumstances a reoperation may be indicated, such as in the presence of

a retained disc fragment. In most cases, however, it appears that SCS is preferred when additional surgery is not definitively indicated to correct the pain generator. For patients who do not have progressive and debilitating neurological deficits or gross spinal instability, SCS should be considered prior to a second or subsequent back surgery. It can also be used for patients who are not candidates for back surgery due to age or comorbidities.

Apart from FBSS, other spinal pain conditions are treated with SCS, including lumbar spinal stenosis. Like FBSS, this condition is often treated at first with medications, physical therapy, epidural steroid injections, and surgery. A majority of spinal stenosis patients have positive surgical outcomes.[19] However, patients who fail to get relief or who are not surgical candidates have been successfully treated with SCS.[20] The therapy appears to be most effective in patients who have moderate or mild spinal stenosis, a positive exercise treadmill test, and pain mostly located in the legs.

SCS has also been employed to treat intractable pain originating in the cervical spine. Patients with such pain often undergo multiple spinal surgeries before being considered for SCS and their symptoms may be linked to neuropathic pain syndromes. Cervical SCS has provided as many as 80% to 90% of these patients with paresthesia in their painful body areas.[21] Stimulation with retrograde leads at cervical spine levels has also been used for a range of pain symptoms, such as occipital pain, jaw pain due to temporal mandibular joint disease, and diffusing pain in the neck, shoulders, and upper extremities. In such cases, adequate paresthesia coverage has been observed in 70% to 80% of patients.[21]

In spite of the technical advances in SCS leads, the ideal lead configuration for FBSS patients is still subject to debate. FBSS patients may be effectively treated with two types of SCS leads: paddle leads that are inserted into the epidural space via a laminotomy, or wire-like leads that are placed using a percutaneous approach. The choice of leads depends on the circumstances of each case. Paddle leads are more energy efficient and appear to have a lower incidence of migration.[22] It is preferred for patients with suspected scarring of the epidural space at the level of insertion, patients with extensive orthopedic hardware in the spine, and patients with high-energy requirements (thus reducing the battery life of the generator), although this may be less of an issue with the advent of rechargeable neurostimulators.

Because paddle leads usually involve a more invasive laminotomy that requires the service of spine surgeons, percutaneous leads are more commonly used. Recent studies have also raised concerns regarding a higher risk of fracture of the paddle leads compared to the percutaneous leads.[23] Furthermore, improved anchoring techniques for percutaneous leads may make the difference in migration rate less significant.[24] The use of multiple contact leads is recommended since the neural targets for FBSS patients appear to change over time.[25] One study suggests that a single percutaneous lead placed on the physiological midline appeared to provide better results than dual percutaneous leads placed in parallel.[26] However, controversy exists as an argument can be made that dual leads provide better programmability and may be less affected by off-midline migrations.

As a technology-based therapy, the initial costs of SCS can be substantial. However, FBSS or other chronic pain patients who are treated with the therapy generally require less follow-up care than similar patients treated with conventional medical management. This can result in a sizable reduction in health resource utilization and make SCS less expensive than conventional treatments over time.[27–29]

NEUROPATHIC PAIN CONDITIONS

Neuropathic pain is any pain condition where the pain experienced is due to the peripheral or central nervous system processing somatosensory signals inappropriately. In chronic neuropathic pain, the cause of the injury may have been resolved but pain continues. It is generally refractory to conservative medical management, particularly to medications. This has given neurostimulation an important role in providing pain relief to patients who would otherwise suffer debilitating chronic pain.

COMPLEX REGIONAL PAIN SYNDROME

Complex regional pain syndrome (CRPS) is a neuropathic disorder that is frequently treated with neurostimulation. CRPS is accompanied by sensory and autonomic dysfunction and may respond poorly to conventional treatments such as physical therapy and rehabilitation, medical management, or sympathetic nerve blocks. The phenomena may present as CRPS-I (formerly known as reflex sympathetic dystrophy, RSD) and CRPS-II (often referred to as causalgia), with a key difference that causalgia is associated with the evidence of a specific peripheral nerve injury. Recently published data indicate that CRPS-I is related to the loss of small diameter nerve fibers (C- and A-δ), countering notions that the disease is generated by the brain or psychiatric disturbances.[30]

Considerable medical literature, mostly in the form of case series, has suggested that SCS has a positive effect on CRPS-I and results in reductions in pain, analgesic use, and functional impairment.[31–33] Around 50% to 60% of CRPS patients treated with SCS report that their pain has been reduced by at least one-half. The pain-relief effect of SCS for such patients is apparently not related to changes in blood flow.[34] CRPS-I also responds favorably to peripheral nerve stimulation with pain relief and improved activity levels in patients whose disease is limited to a single peripheral nerve distribution.[35]

A recent randomized, controlled study performed to compare treatment of CRPS-I using SCS and physical therapy vs. physical therapy alone showed that the SCS group experienced significant reductions in pain compared to the physical therapy group.[36] However, at 5 years, follow-up data indicated that this difference was no longer statistically significant. The original study and the follow-up data have been criticized for its methodology and its use of outdated technologies on patients with advanced disease, factors that may have affected the long-term outcomes of SCS. It is paramount to treat patients early in the disease course and use technology that covers the entire affected limb to achieve favorable outcomes. A meta-analysis of CRPS literature suggests that early intervention and combining SCS with physical therapy and rehabilitation are associated with better outcomes.[12] For this reason, experts have recommended that SCS should be considered for CRPS-I patients no later than four months after the failure of conservative treatment.[37] Cost benefit analysis studies show that SCS, despite the high cost of the hardware and surgical care, is cost effective as compared to alternative treatments, and actually saves money in the long run due to the savings in healthcare resources utilization.[12,27–29]

POST-HERPETIC NEURALGIA

Post-herpetic neuralgia (PHN) is another neuropathic condition that may respond to SCS. The pain of PHN is believed to be due to deafferentation of spinal neurons. Although early use of SCS to relieve PHN pain is associated with positive results,[38] the application of the therapy has subsequently produced mixed results. However, a recent investigation found that patients with PHN experienced pain reduction and functional improvement with SCS.[39] Furthermore, pain from trigeminal PHN has reportedly been controlled successfully with peripheral nerve stimulation.[40]

PERIPHERAL NEUROPATHY

Neurostimulation has been used to treat pain of peripheral neuropathies of varying etiologies, including diabetic neuropathy and postamputation syndromes such as phantom limb and stump pain. While the early use of SCS for diabetic neuropathy produced mixed results, more recent efforts have been encouraging. Patients with diabetic neuropathy responded to SCS with increased exercise tolerance and significant pain relief.[41,42] Peripheral nerve stimulation has also been used.[43] Interestingly, one case report showed significant pain relief and better blood glucose control after the use of thoracic SCS in diabetic neuropathy.[44] Compromise of microcirculatory blood flow and persistence of the neuropathic pain are frequent complications of advanced diabetes. SCS may provide improved pain control, increased skin blood flow, and possible limb salvage in patients who failed conservative or surgical treatment. The published data on the use of neurostimulation for postamputation neuropathic pain are limited to case reports that group these different pain categories together, making it hard to evaluate the success of SCS in each type of pain individually.

OCCIPITAL NEURALGIA

First-line approaches for treating occipital neuralgia include medications, physical therapy, biofeedback, psychotherapy, and regional nerve blocks. Neurostimulation should only be used when these treatments have failed to provide long-term pain relief and the pain severely compromises the patient's quality of life. Neurostimulation should be considered prior to any destructive nerve procedures such as neurectomy of the greater and lesser occipital nerves or C2 or C3 ganglionectomies. These latter procedures are commonly performed despite their lack of long-term benefits. A similar approach to treatment with neurostimulation should be employed for patients suffering from supraorbital, infraorbital, and auriculotemporal pain. Peripheral nerve stimulation has been successful in managing intractable migraines and occipital neuralgia, with a majority of patients reporting long-term reductions in pain of over 50%.[45,46] A novel technique to treat occipital neuralgia is use of two surgical paddle leads placed across the back of the neck at the level of the atlanto-occipital joints has been described.[47] Such technique enhances the stability of the peripheral nerve stimulator and decreases the chance of migration.

Peripheral nerve field stimulation (PNFS) or subcutaneous neurostimulation refers to neurostimulation

delivered through leads placed in the subcutaneous tissue in the region of maximum pain. It has been used with success in treating neuropathic pain of the head, neck, face, back, groin, and abdomen.[40,48] Additionally, it has provided patients with pain relief from intractable ilioinguinal neuralgia.[49] In some cases, the stimulation can be applied for 1 to 2 hours per day and produce relief from pain that lasts from 12 to 24 hours.[50] PNFS involves a complex decision making process in which the physician must obtain a history of pain in a nerve distribution, examine and evaluate the appropriate innervation and dermatomes, and develop a treatment algorithm with a goal of pain reduction. In cases where acceptable conservative measures fail to give acceptable results, a lead is placed in proximity to the affected nerve. The lead can be placed by needle delivery or by cut-down and direct visualization. In the past the placement of a peripheral nerve device required a complicated surgical procedure with a fascial graft. Newer lead technology, improved programming, and a better understanding of nerve targets have simplified this procedure. The risks of this technique are minimal and trialing is performed at very low risk. This procedure should be considered early in the continuum of care.

NEUROSTIMULATION FOR ISCHEMIC PAIN

Neurostimulation has been used to control pain caused by a variety of ischemic conditions and has significant value for intractable angina or peripheral vascular disease patients when reconstructive vascular surgeries are not possible or are contraindicated due to comorbidities. It is also a valuable option for patients with small vessel disease where revascularization is not possible. The therapy has been used extensively for ischemic pain in Europe, where it is the leading indication for the therapy.[51]

PERIPHERAL VASCULAR DISEASE

Pain from peripheral vascular disease may have both nociceptive and neuropathic pain components, the latter becoming more prevalent as peripheral neurons degenerate during the progression of the disease. The use of SCS for peripheral vascular disease is associated with an increase in capillary blood flow and skin temperature, reduced pain, enhanced healing of skin ulcers less than 3 centimeters, and increased limb salvage rates when used to treat critical limb ischemia.[52–54] A recent meta-analysis revealed that patients with critical limb ischemia who were treated with SCS experienced greater pain reduction and higher limb salvage rates than the cohorts treated with conservative therapies.[54] Such improvements in limb salvage appear to be related to a vasodilatation effect produced by SCS. Consequently, transcutaneous oxygen tension measurement levels ($TcpO_2$) became an important screening and prognostic tool to identify patients who may benefit from permanent SCS implant. A review of 258 peripheral vascular disease patients showed that the limb salvage rate in those who had low baseline $TcpO_2$ levels (<10 mm/hg) was 77% at 18 months, vs. 90% in those who had higher baseline $TcpO_2$ levels (10 mm/hg to 30 mm/hg).[54] Treatment outcomes were the same regardless of whether the patients had a diabetic or nondiabetic disease. In a study involving 150 patients with critical limb ischemia, an increase in $TcpO_2$ levels of greater than 50% during the first two months of SCS treatment was found to be a predictor of long-term pain relief and limb salvage.[55]

Neurostimulation is suited for patients who have a Fontaine classification of III or IV (Fontaine classification: I = asymptomatic; II = intermittent claudication; II-a = pain free, claudication walking more than 200 meters; II-b = pain free, claudication walking less than 200 meters; III = rest/nocturnal pain; IV = necrosis/gangrene). A primary goal when using neurostimulation to treat critical limb ischemia is limb salvage, as well as reducing pain and medication use and improving quality of life. When used to treat critical limb ischemia, SCS has resulted in pain reductions that often correlate with improved limb salvage. Patients with this condition should have adequate collateral blood flow in their affected areas in order to be considered for the therapy. Patients should not have had a prior amputation in the targeted limb. Neurostimulation is preferable when revascularization is contraindicated or has a low likelihood of success. It is also helpful for patients who have ulcers greater than 3 cm^2. Gangrene is a relative contraindication because of the increased risk of systemic and neuroaxial infection. In focal gangrene of the digits, SCS may be helpful in revascularization and reduction of the size of the required limb amputation. In such situations, close internal medicine or infectious disease monitoring should accompany the implant. The measuring of $TcpO_2$ levels may help identify patients who could benefit from neurostimulation, but the difficulty of performing this measurement in this patient population may preclude it from being a practical diagnostic tool in clinical practice.

ANGINA

Many European studies have confirmed the ability of neurostimulation, especially SCS, to mitigate the symptoms of angina. SCS reduces pain, decrease nitrate requirements, and promotes exercise capacity.[56,57] About 80% of angina patients treated with SCS experienced fewer angina attacks and improved quality of life,[58–60] and some studies have shown that patients maintain such results for up to 5 years after therapy.[61,62] SCS also appears to improve blood flow and reduce myocardial ischemia,[63,64] possibly through the creation of collateral circulation as a result of increased exercise.[65] Despite early concerns that SCS might mask the symptoms of serious cardiac events, the therapy does not prevent patients from experiencing the warning signs of acute myocardial infarctions.[66]

The ability of neurostimulation to improve blood flow suggests that it might be used earlier in the treatment continuum for some ischemic pain indications. Whether neurostimulation can be used in lieu of vascular bypass or reconstructive surgery depends on whether these surgeries are feasible and prudent and, to some extent, on the size of the vessels in question. Small vessel disease may not be amenable to a surgical approach and may be more appropriately treated with neurostimulation, as this therapy has been shown to improve microcirculation. The vasodilatation effect of neurostimulation may also make it useful for treating persistent ischemia that diminishes the patient's function without the accompanied pain. Currently, neurostimulation is underused as a treatment for ischemic pain in the United States. Based on its history of use in Europe, outcome investigations of neurostimulation for ischemic pain are strongly encouraged. Its promise for reducing such pain and improving function should make this type of research a priority, as significant numbers of patients with cardiac, and/or peripheral vascular, ischemia may benefit from this treatment option.

NEUROSTIMULATION FOR VISCERAL PAIN

The treatment of visceral pain is one of the newer applications of neurostimulation therapy. Visceral pain can result from a number of conditions, such as those involving the abdomen and pelvis. Pancreatitis, interstitial cystitis, and rectal conditions are common sources of visceral pain and may be associated with other dysfunction such as urgency or incontinence. Visceral pain syndromes are often poorly localized and usually with nonspecific pain patterns.[67] Such pain syndromes are often associated with relatively strong autonomic responses that may lead to somatic sensitization. The pain produced by these conditions is not necessarily related to visceral injuries. Current treatments for chronic visceral abdominal pain, such as various nerve blocks and radiofrequency ablations, rarely produce long-term pain relief.

SCS is supported by laboratory observations in the treatment of abdominal and pelvic pain and hyperalgesia induced by repeated visceral distensions.[68–70] The mechanisms by which SCS suppresses visceral pain may be multifactorial and need to be further investigated.[71] One of the challenges of neurostimulation is that relatively few afferent nerves join the spinal cord from visceral areas.[72] Only a small number of afferents in the lower thoracic spinal cord originate in the viscera. The proportion of these nerves in the sacral regions may not be much different. It is therefore difficult to stimulate a part of the cord to cover visceral pain without stimulating nonvisceral nerves. Nonetheless, stimulation of spinal nerve structures has been successful in reducing visceral pain in a number of abdominal and pelvic syndromes,[73–75] such as refractory vulvar pain,[76] mesenteric ischemia,[77] esophageal pain,[78] and pain resulting from abdominal surgeries.[79] Case series studies suggest that SCS for abdominal and pelvic visceral pain is associated with improvements in pain scores,[71,75,79–82] functional capacity,[80] and the opioid use.[79,80,82] SCS may also improve function and ease pain in patients with irritable bowel syndrome.[83] Using SCS for visceral pelvic pain does not appear to result in neural damage, even when applied over a long period of time. However, it is not clear from the data of these case reports and case series how many patients actually proceeded from successful trials to SCS implant and if there is any long-term efficacy.

Of special note is the use of neurostimulation for interstitial cystitis. As many as 1 million people in the United States may suffer from interstitial cystitis. This debilitating pain syndrome is characterized by urinary urgency, frequent urination, and chronic pelvic pain, and it is often accompanied by hyperalgesia and allodynia. It is more of a neuropathic condition than a bladder disorder. The few treatments for interstitial cystitis, such as the use of anti-inflammatory drugs, caustic agents, or surgery, often only work temporarily or even worsen a patient's symptoms. However, neurostimulation of the sacral nerve roots has been successfully used in alleviating pain, urinary urgency, and voiding frequency of the condition.[84–87] In a prospective study, 15

patients were treated with S3 stimulation and their average voiding volume increased by over 50% while their average frequency of daytime urination was cut approximately in half.[86] S3 stimulation has also helped to normalize urothelial cell activity in the bladder that the disorder has altered.[87] Results such as these have led some physicians to propose using neurostimulation earlier in the care for interstitial cystitis and similar pelvic disorders since it would spare patients from potentially damaging procedures such as hydrodistention, bladder installations, and cystectomies.[88] A lumbar retrograde approach to lead placement appears to limit lead migrations and provide easier coverage of sacral nerves than the transforaminal approach.[89] Stimulating the sacral nerves has also been successful in reducing fecal incontinence,[90,91] as well as the pain, urgency, frequency, and voiding problems of other urinary disorders.[92,93] Considering the strength of evidence, the use of neurostimulation should be encouraged prior to cystectomy.

Like many other new therapies, the use of neurostimulation for visceral pain may be well utilized in clinical settings yet underreported in the medical literature. This lack of published data justifiably makes many healthcare professionals reluctant to support the application of this therapy, even though it may offer hope to patients with devastating pain conditions that are unresponsive to other "established" treatments. Neurostimulation has the advantage of being nondestructive and reversible with relatively few complications or adverse events. This promising therapy calls for outcome investigations, particularly in the form of randomized, controlled studies, to establish evidence based clinical practice so patients with devastating visceral pain can benefit from this potentially extremely useful modality.

FUTURE DIRECTIONS

The current clinical application of neurostimulation is exciting and offers hope to patients who are at or near the end of the treatment algorithm. Evidence supports that neurostimulation should move up in the treatment algorithms of many conditions and be offered earlier in the course of care. New developments in technology have been critical to improving outcomes over the past decade. Currently, research is directed to making devices smaller, improving the number of contacts available per lead, making the device MRI compatible, allowing for bluetooth or other wireless communication, reducing the recharge burden, improving lead delivery to different spinal targets, and assessing the efficacy of neuromodulation in different disease states.

CONCLUSIONS

Neuromodulation is a critical part of the treatment algorithm for those suffering from neuropathic pain. The clinical efficacy for SCS is well proven for FBSS and CRPS. Evidence supporting SCS is also very strong for peripheral neuropathy and ischemic pain from peripheral vascular disease and angina. The use of peripheral nerve stimulation is very positive for neuralgias of occipital nerve, supraorbital nerve, inguinal nerve, and intercostal nerve. The authors encourage future prospective studies on neurostimulation for visceral pain syndromes and other new indications. With appropriate patient selection, neurostimulation is a valuable option to reduce pain, optimize function, improve quality of life, and decrease healthcare costs in many of those suffering debilitating pain conditions.

REFERENCES

1. Shealy CN, Mortimer JT, Reswick JB. Electrical inhibition of pain by stimulation of the dorsal columns: preliminary clinical report. *Anesth Analg*. 1967;46:489–491.

2. Wilkinson HA. *The Failed Back Surgery Syndrome: Etiology and Therapy*. 2nd ed. Philadelphia, PA: Harper and Row; 1991.

3. Villavicencio AT, Leveque JC, Rubin L, Bulsara K, Gorecki JP. Laminectomy versus percutaneous electrode placement for spinal cord stimulation. *Neurosurgery*. 2000; 46:399–405.

4. Barolat G, Sharan AD. Future trends in spinal cord stimulation. *Neurol Res*. 2000;22:279–284.

5. Kumar K, Toth C, Nath RK, Laing P. Epidural spinal cord stimulation for treatment of chronic pain—some predictors of success. A 15-year experience. *Surg Neurol*. 1998; 50:110–120.

6. Van Buyten JP. Neurostimulation for chronic neuropathic back pain in failed back surgery syndrome. *J Pain Symptom Manage*. 2006;31:S25–29.

7. Devulder J, De Laat M, Van Bastelaere M, Rolly G. Spinal cord stimulation: a valuable treatment for chronic failed back surgery patients. *J Pain Symptom Manage*. 1997;13:296–301.

8. Barolat G. A prospective multicenter study to assess the efficacy of spinal cord stimulation utilizing a multi-channel radio-frequency system for the treatment of intractable low back and lower extremity pain. Initial considerations and methodology. *Neuromodulation*. 1999; 2:179–183.

9. Burchiel KJ, Anderson VC, Brown FD, et al. Prospective, multicenter study of spinal cord stimulation for relief of chronic back and extremity pain. *Spine*. 1996;21:2786–2794.

10. North RB, Guarino AH. Spinal cord stimulation for failed back surgery syndrome: technical advances, patient selection and outcome. *Neuromodulation*. 1999;2:171–178.

11. Van Buyten JP, Van Zundert J, Vueghs P, Vanduffel L. Efficacy of spinal cord stimulation: 10 years of experience in a pain centre in Belgium. *Eur J Pain*. 2001;5:299–307.

12. Taylor RS. Spinal cord stimulation in complex regional pain syndrome and refractory neuropathic back and leg pain/failed back surgery syndrome: results of a systematic review and meta-analysis. *J Pain Symptom Manage*. 2006; 31:S13–S19.

13. North RB, Kidd DH, Farrokhi F, Piantadosi SA. Spinal cord stimulation versus repeated lumbosacral spine surgery for chronic pain: a randomized, controlled trial. *Neurosurgery*. 2005;56:98–106.

14. Kumar K, Taylor R, Jacques L, et al. Spinal cord stimulation versus conventional medical management for neuropathic pain: a multicentre randomized controlled trial in patients with failed back surgery syndrome. *Pain*. 2007; 132:179–188.

15. Barolat G. Epidural spinal cord stimulation: anatomical and electrical properties of the intraspinal structures relevant to spinal cord stimulation and clinical correlations. *Neuromodulation*. 1998;1:63–71.

16. Barolat G, Oakley JC, Law JD, North RB, Ketcik B, Sharan A. Epidural spinal cord stimulation with a multiple electrode paddle lead is effective in treating intractable low back pain. *Neuromodulation*. 2001;4:59–66.

17. Deer T, Krames E, Hassenbusch S, et al. Management of IT catheter-tip inflammatory masses: an updated 2007 consensus statement from an expert panel. *Neuromodulation*. 2008;11:77–91.

18. Bernstein CA, Paicius RM, Barkow SH. Spinal cord stimulation in conjunction with peripheral nerve field stimulation for the treatment of low back and leg pain: a case series. *Neuromodulation*. 2008;11:116–123.

19. Chandler GS 3rd, Nixon B, Stewart LT, Love J. Dorsal column stimulation for lumbar spinal stenosis. *Pain Physician*. 2003;6:113–118.

20. Amundsen T, Weber H, Nordal HJ, Magnaes B, Abdelnoor M, Lilleas F. Lumbar spinal stenosis: conservative or surgical management?: a prospective 10-year study. *Spine*. 2000;25:1424–1435.

21. Barolat G. Experience with 509 plate electrodes implanted epidurally from C1 to L1. *Stereotact Funct Neurosurg*. 1993;61:60–79.

22. North RB, Kidd DH, Olin JC, Sieracki JM. Spinal cord stimulation electrode design: prospective, randomized, controlled trial comparing percutaneous and laminectomy electrodes-part I: technical outcomes. *Neurosurgery*. 2002;51: 381–390.

23. Rosenow JM, Stanton-Hicks M, Rezai AR, Henderson JM. Failure modes of spinal cord stimulation hardware. *J Neurosurg Spine*. 2006;5:183–190.

24. Henderson JM, Schade CM, Sasaki J, Caraway DL, Oakley JC. Prevention of mechanical failures in implanted spinal cord stimulation systems. *Neuromodulation*. 2006;9: 183–191.

25. Sharan A, Cameron T, Barolat G. Evolving patterns of spinal cord stimulation in patients implanted for intractable low back and leg pain. *Neuromodulation*. 2002;5:167–179.

26. North RB, Kidd DH, Olin J, et al. Spinal cord stimulation for axial low back pain: a prospective, controlled trial comparing dual with single percutaneous electrodes. *Spine*. 2005;30:1412–1418.

27. Mekhail NA, Aeschbach A, Stanton-Hicks M. Cost benefit analysis of neurostimulation for chronic pain. *Clin J Pain*. 2004;20:462–468.

28. Taylor RS, Taylor RJ, Van Buyten JP, Buchser E, North R, Bayliss S. The cost effectiveness of spinal cord stimulation in the treatment of pain: a systematic review of the literature. *J Pain Symptom Manage*. 2004;27:370–378.

29. Kumar K, Malik S, Demeria D. Treatment of chronic pain with spinal cord stimulation versus alternative therapies: cost-effectiveness analysis. *Neurosurgery*. 2002;51:106–115.

30. Oaklander AL, Rissmiller JG, Gelman LB, Zheng L, Chang Y, Gott R. Evidence of focal small-fiber axonal degeneration in complex regional pain syndrome-I (reflex sympathetic dystrophy). *Pain*. 2006;120:235–243.

31. Harke H, Gretenkort P, Ladleif HU, Rahman S. Spinal cord stimulation in sympathetically maintained complex regional pain syndrome type I with severe disability. A prospective clinical study. *Eur J Pain*. 2005;9:363–373.

32. Oakley JC, Weiner RL. Spinal cord stimulation for complex regional pain syndrome: a prospective study of 19 patients at two centers. *Neuromodulation*. 1999;2:47–50.

33. Barolat G, Schartzman R, Woo R. Epidural spinal cord stimulation in the management of reflex sympathetic dystrophy. *Stereotact Funct Neurosurg*. 1989;53:29–39.

34. Kemler MA, Barendse GA, van Kleef M, Egbrink MG. Pain relief in complex regional pain syndrome due to spinal cord stimulation does not depend on vasodilatation. *Anesthesiology*. 2000;92:1653–1660.

35. Hassenbusch SJ, Stanton-Hicks M, Schoppa D, Walsh JG, Covington EC. Long-term results of peripheral nerve stimulation for reflex sympathetic dystrophy. *J Neurosurg*. 1996;84:415–423.

36. Kemler MA, Barendse GA, van Kleef M, et al. Spinal cord stimulation in patients with chronic reflex sympathetic dystrophy. *N Engl J Med*. 2000;343:618–624.

37. Stanton-Hicks M. Complex regional pain syndromes: manifestations and the role of neurostimulation in its management. *J Pain Symptom Manage*. 2006;31:S20–24.

38. Meglio M, Cioni B, Prezioso A, Talamonti G. Spinal cord stimulation (SCS) in the treatment of postherpetic pain. *Acta Neurochir Suppl (Wien)*. 1989;46:65–66.

39. Harke H, Gretenkort P, Ladleif HU, Koester P, Rahman S. Spinal cord stimulation in postherpetic neuralgia

and in acute herpes zoster pain. *Anesth Analg*. 2002;94:694–700.

40. Johnson MD, Burchiel KJ. Peripheral stimulation for treatment of trigeminal postherpetic neuralgia and trigeminal posttraumatic neuropathic pain: a pilot study. *Neurosurgery*. 2004;55:135–141.

41. Tesfaye S, Watt J, Benbow SJ, Pang KA, Miles J, MacFarlane IA. Electrical spinal-cord stimulation for painful diabetic peripheral neuropathy. *Lancet*. 1996;348:1698–1701.

42. Daousi C, Benbow SJ, MacFarlane IA. Electrical spinal cord stimulation in the long-term treatment of chronic painful diabetic neuropathy. *Diabet Med*. 2005;22:393–398.

43. Hamza MA, White PF, Craig WF, et al. Percutaneous electrical nerve stimulation: a novel analgesic therapy for diabetic neuropathic pain. *Diabetes Care*. 2000;23:365–370.

44. Kapural L, Hayek SM, Stanton-Hicks M, Mekhail N. Decreased insulin requirements with spinal cord stimulation in a patient with diabetes. *Anesth Analg*. 2004;98:745–746.

45. Weiner RL. Occipital neurostimulation (ONS) for treatment of intractable headache disorders. *Pain Med*. 2006;7:S137–139.

46. Slavin KV, Nersesyan H, Wess C. Peripheral neurostimulation for treatment of intractable occipital neuralgia. *Neurosurgery*. 2006;58:112–119.

47. Kapural L, Mekhail N, Hayek SM, Stanton-Hicks M, Malak O. Occipital nerve electrical stimulation via the midline approach and subcutaneous surgical leads for treatment of severe occipital neuralgia: a pilot study. *Anesth Analg*. 2005;101:171–174.

48. Paicius RM, Bernstein CA, Lempert-Cohen C. Peripheral nerve field stimulation in chronic abdominal pain. *Pain Physician*. 2006;9:261–266.

49. Stinson LW, Roderer GT, Cross NE, Davis BE. Peripheral subcutaneous electrostimulation for control of intractable post-operative inguinal pain: a case report series. *Neuromodulation*. 2001;4:99–104.

50. Goroszeniuk T, Kothari S, Hamann W. Subcutaneous neuromodulation implant targeted at the site of pain. *Reg Anesth Pain Med*. 2006;31:168–171.

51. Deer TR, Raso LJ. Spinal cord stimulation for refractory angina pectoris and peripheral vascular disease. *Pain Physician*. 2006;9:347–352.

52. Ghajar AW, Miles JB. The differential effect of the level of spinal cord stimulation on patients with advanced peripheral vascular disease in the lower limbs. *Br J Neurosurg*. 1998;12:402–408.

53. Linderoth B. Spinal cord stimulation in ischemia and ischemic pain: possible mechanisms of action. In: Horsch S, Claeys L, eds. *Spinal Cord Stimulation. An Innovative Method in the Treatment of PVD and Angina*. Darmstadt: Steinkopff Verlag; 1995:19–35.

54. Ubbink DT, Vermeulen H, Spincemaille GH, Gersbach PA, Berg P, Amann W. Systematic review and meta-analysis of controlled trials assessing spinal cord stimulation for inoperable critical leg ischaemia. *Br J Surg*. 2004;91:948–955.

55. Petrakis IE, Sciacca V. Spinal cord stimulation in critical limb ischemia of the lower extremities: our experience. *J Neurosurg Sci*. 1999;43:285–293.

56. Mannheimer C, Eliasson T, Andersson B, et al. Effects of spinal cord stimulation in angina pectoris induced by pacing and possible mechanisms of action. *BMJ*. 1993;307:477–480.

57. Greco S, Auriti A, Fiume D, et al. Spinal cord stimulation for the treatment of refractory angina pectoris: a two-year follow-up. *Pacing Clin Electrophysiol*. 1999;22:26–32.

58. Hautvast RW, DeJongste MJ, Staal MJ, van Gilst WH, Lie KI. Spinal cord stimulation in chronic intractable angina pectoris: a randomized, controlled efficacy study. *Am Heart J*. 1998;136:1114–1120.

59. Eliasson T, Augustinsson L, Mannheimer C. Spinal cord stimulation in severe angina pectoris—presentation of current studies, indications, and clinical experience. *Pain*. 1996;65:169–179.

60. DeJongste MJ. Spinal cord stimulation for ischemic heart disease. *Neurol Res*. 2000;22:293–298.

61. TenVaarwerk I, Jessurun G, DeJongste MJ, et al. Clinical outcome of patients treated with spinal cord stimulation for therapeutically refractory angina pectoris. *Heart*. 1999;82:82–88.

62. Ekre O, Eliasson T, Norrsell H, Wahrborg P, Mannheimer C. Long-term effects of spinal cord stimulation and coronary artery bypass grafting on quality of life and survival in the ESBY study. *Eur Heart J*. 2002;23:1938–1945.

63. Chauhan A, Mullins PA, Thursraisingham SI, Taylor G, Petch MC, Schofeld PM. Effect of transcutaneous electrical nerve stimulation on coronary blood flow. *Circulation*. 1994;89:694–702.

64. Mobilia G, Zuin G, Zanco P, et al. Effects of spinal cord stimulation on regional myocardial blood flow in patients with refractory angina. A positron emission tomography study. *G Ital Cardiol*. 1998;28:1113–1119.

65. Diedrichs H, Zobel C, Theissen P, et al. Symptomatic relief precedes improvement of myocardial blood flow in patients under spinal cord stimulation. *Curr Control Trials Cardiovasc Med*. 2005;6:7.

66. Murray S, Carson KG, Ewings PD, Collins PD, James MA. Spinal cord stimulation significantly decreases the need for acute hospital admission for chest pain in patients with refractory angina pectoris. *Heart*. 1999;82:89–92.

67. Cervero F. Neurophysiology of gastrointestinal pain. *Baillieres Clin Gastroenterol*. 1988;2:183–199.

68. Palecek J. The role of dorsal columns pathway in visceral pain. *Physiol Res*. 2004;53(suppl 1):S125–S130.

69. Greenwood-Van Meerveld B, Johnson AC, Foreman RD, Linderoth B. Spinal cord stimulation attenuates visceromotor reflexes in a rat model of post-inflammatory colonic hypersensitivity. *Auton Neurosci*. 2005;122:69–76.

70. Qin C, Lehew RT, Khan KA, Wienecke GM, Foreman RD. Spinal cord stimulation modulates intraspinal colorectal viscereroreceptive transmission in rats. *Neurosci Res*. 2007;58:58–66.

71. Krames ES, Foreman R. Spinal cord stimulation modulates visceral nociception and hyperalgesia via the spinothalamic tracts and the postsynaptic dorsal column pathways: a literature review and hypothesis. *Neuromodulation*. 2007;10:224–237.

72. Cervero F, Connell LA, Lawson SN. Somatic and visceral primary afferents in the lower thoracic dorsal root ganglia of the cat. *J Comp Neurol*. 1984;228:422–431.

73. Peters KM. Neuromodulation for the treatment of refractory interstitial cystitis. *Rev Urol*. 2002;4:S36–S43.

74. Elabbady AA, Hassouna MM, Elhilali MM. Neural stimulation for chronic voiding dysfunctions. *J Urol*. 1994; 152:2076–2080.

75. Khan YN, Raza SS, Khan EA. Spinal cord stimulation in visceral pathologies. *Pain Med*. 2006;7:S121–S125.

76. Whiteside JL, Walters MD, Mekhail N. Spinal cord stimulation for intractable vulvar pain. A case report. *J Reprod Med*. 2003;48:821–823.

77. Ceballos A, Cabezudo L, Bovaira M, Fenollosa P, Moro B. Spinal cord stimulation: a possible therapeutic alternative for chronic mesenteric ischemia. *Pain*. 2000;87:99–101.

78. Jackson M, Simpson KH. Spinal cord stimulation in a patient with persistent oesophageal pain. *Pain*. 2004; 112:406–408.

79. Khan YN, Raza SS, Khan EA. Application of spinal cord stimulation for the treatment of abdominal visceral pain syndromes: case reports. *Neuromodulation*. 2005;8:14–27.

80. Kapural L, Narouze SN, Janicki TI, Mekhail N. Spinal cord stimulation is an effective treatment for the chronic intractable visceral pelvic pain. *Pain Med*. 2006; 7:440–443.

81. Tiede JM, Ghazi SM, Lamer TJ, Obray JB. The use of spinal cord stimulation in refractory abdominal visceral pain: case reports and literature review. *Pain Pract*. 2006; 6:197–202.

82. Kapural L, Rakic M. Spinal cord stimulation for chronic visceral pain secondary to chronic non-alcoholic pancreatitis: a case report. *Clin Gastroenterol Hepatol*. 2008;42:750–751.

83. Krames E, Mousad DG. Spinal cord stimulation reverses pain and diarrheal episodes of irritable bowel syndrome: a case report. *Neuromodulation*. 2004;7:82.

84. Feler CA, Whitworth LA, Brookoff D, Powell R. Recent advances: sacral nerve root stimulation using a retrograde method of lead insertion for the treatment of pelvic pain due to interstitial cystitis. *Neuromodulation*. 1999;2:211–216.

85. Comiter CV. Sacral neuromodulation for symptomatic treatment of refractory interstitial cystitis: a prospective study. *J Urol*. 2003;169:1369–1373.

86. Maher CF, Carey MP, Dwyer PL, Schluter PI. Percutaneous sacral nerve root neuromodulation for intractable interstitial cystitis. *J Urol*. 2001;165:884–886.

87. Chai TC, Zhang C, Warren JW, Keay S. Percutaneous sacral third nerve root neurostimulation improves symptoms and normalizes urinary HB-EGF levels and antiproliferative activity in patients with interstitial cystitis. *Urology*. 2000;55:643–646.

88. Sherman ND, Amundsen CL. Current and future techniques of neuromodulation for bladder dysfunction. *Curr Urol Rep*. 2007;8:448–454.

89. Alo KM, Gohel R, Corey CL. Sacral nerve root stimulation for the treatment of urge incontinence and detrusor dysfunction utilizing a cephalocaudal intraspinal method of lead insertion: a case report. *Neuromodulation*. 2001;4:53–58.

90. Ganio E, Luc AR, Clerico G, Trompetto M. Sacral nerve stimulation for treatment of fecal incontinence: a novel approach for intractable fecal incontinence. *Dis Colon Rectum*. 2001;44:619–629.

91. Kenefick NJ, Vaizey CJ, Cohen RC, Nicholls RJ, Kamm MA. Medium-term results of permanent sacral nerve stimulation for faecal incontinence. *Br J Surg*. 2002;89:896–901.

92. Bemelmans BL, Mundy AR, Craggs MD. Neuromodulation by implant for treating lower urinary tract symptoms and dysfunction. *Eur Urol*. 1999;36:81–91.

93. Shaker HS, Hassouna M. Sacral root neuromodulation in idiopathic nonobstructive chronic urinary retention. *J Urol*. 1998;159:1476–1478.